Claims

1. A purified polypeptide that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, wherein said polypeptide specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), ASPC-1 (ATCC Accession No. CRL-1682), or BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells.

2. The purified polypeptide of claim 1, wherein said polypeptide binds to ASPC-1 (ATCC Accession No. CRL-1682) and BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a stomach adenocarcinoma, colorectal adenocarcinoma, squamous cell lung carcinoma, lung adenocarcinoma, squamous cell carcinoma of the esophagus, adenocarcinoma of the pancreas, adenocarcinoma of the prostate, ductal carcinoma of the breast, lobular carcinoma of the breast, adenocarcinoma of the ovary, or adenocarcinoma of the uterus cell.

3. The purified polypeptide of claim 1, wherein said polypeptide binds to HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), ASPC-1 (ATCC Accession No. CRL-1682), and BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a stomach adenocarcinoma, colorectal adenocarcinoma, squamous cell lung carcinoma, lung adenocarcinoma, squamous cell carcinoma of the esophagus, adenocarcinoma of the pancreas, urothel carcinoma of the urinary bladder, renal cell carcinoma of the kidney, adenocarcinoma of the prostate, ductal carcinoma of the breast, lobular carcinoma of the breast, adenocarcinoma of the ovary, or adenocarcinoma of the uterus cell.

4. The purified polypeptide of claim 1, wherein said polypeptide binds to CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169) and COLO-206F (DSMZ Accession No. ACC 21) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a colorectal adenocarcinoma or adenocarcinoma of the endometrium cell.

5. A purified polypeptide that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, wherein said polypeptide specifically binds to a stomach adenocarcinoma, colorectal adenocarcinoma, squamous cell lung carcinoma, lung adenocarcinoma, squamous cell carcinoma of the esophagus, adenocarcinoma of the pancreas, urothel carcinoma of the urinary bladder, renal cell carcinoma of the kidney, adenocarcinoma of the prostate, ductal carcinoma of the breast, lobular carcinoma of the breast, adenocarcinoma of the ovary, adenocarcinoma of the endometrium, or adenocarcinoma of the uterus cell and not to a non-neoplastic cell.

6. A purified polypeptide that inhibits cell proliferation when bound to a neoplastic cell, but does not inhibit cell proliferation of a non-neoplastic cell, wherein said polypeptide specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), ASPC-1 (ATCC Accession No. CRL-1682), or BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells.

7. The purified polypeptide of claim 6, wherein said polypeptide binds to ASPC-1 (ATCC Accession No. CRL-1682) and BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a stomach adenocarcinoma, colorectal adenocarcinoma, squamous cell lung carcinoma, lung adenocarcinoma, squamous cell carcinoma of the esophagus, adenocarcinoma of the pancreas, adenocarcinoma of the prostate, ductal carcinoma of the breast, lobular carcinoma of the breast, adenocarcinoma of the ovary, or adenocarcinoma of the uterus cell.

8. The purified polypeptide of claim 6, wherein said polypeptide binds to HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), ASPC-1 (ATCC Accession No. CRL-1682), and BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a stomach adenocarcinoma, colorectal adenocarcinoma, squamous cell lung carcinoma, lung adenocarcinoma, squamous cell carcinoma of the esophagus, adenocarcinoma of the pancreas, urothel carcinoma of the urinary bladder, renal cell carcinoma of the kidney, adenocarcinoma of the prostate, ductal carcinoma of the breast, lobular carcinoma of the breast, adenocarcinoma of the ovary, or adenocarcinoma of the uterus cell.

9. The purified polypeptide of claim 6, wherein said polypeptide binds to CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169) and COLO-206F (DSMZ Accession No. ACC 21) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a colorectal adenocarcinoma or adenocarcinoma of the endometrium cell.

10. A purified polypeptide that inhibits cell proliferation when bound to a neoplastic cell, but does not inhibit cell proliferation of a non-neoplastic cell, wherein said polypeptide specifically binds to a stomach adenocarcinoma, colorectal adenocarcinoma, squamous cell lung carcinoma, lung adenocarcinoma, squamous cell carcinoma of the esophagus, adenocarcinoma of the pancreas, urothel carcinoma of the urinary bladder, renal cell carcinoma of the kidney, adenocarcinoma of the prostate, ductal carcinoma of the breast, lobular carcinoma of the breast, adenocarcinoma of the ovary, adenocarcinoma of the endometrium, or adenocarcinoma of the uterus cell and not to a non-neoplastic cell.

11. The purified polypeptide of claim 1, 5, 6, or 10, wherein said polypeptide comprises an antibody or a functional fragment thereof.

12. The purified polypeptide of claim 11, wherein said polypeptide is a functional fragment selected from the group consisting of V_L, V_H, F_V, F_C, Fab, Fab', and $F(ab')_2$.

13. The purified polypeptide of claim 12, wherein said functional fragment comprises a fragment that is substantially identical to the sequence of SEQ ID NO:1 or SEQ ID NO:3.

14. The purified polypeptide of claim 13, wherein said functional fragment comprises a fragment that is substantially identical to a polypeptide comprising amino acids 26-31, 49-51, and 88-95 of SEQ ID NO:1 or amino acids 11-18, 36-43, and 82-90 of SEQ ID NO:3.

15. The purified polypeptide of claim 12, wherein said functional fragment comprises a fragment that is substantially identical to the sequence of SEQ ID NO:5 or SEQ ID NO:7.

16. The purified polypeptide of claim 15, wherein said functional fragment comprises a fragment that is substantially identical to a polypeptide comprising amino acids 26-34, 52-58, and 97-103 of SEQ ID NO:5 or amino acids 11-18, 36-43, and 82-100 of SEQ ID NO:7.

17. The purified polypeptide of claim 12, wherein said functional fragment comprises a fragment that is substantially identical to the sequence of SEQ ID NO:9 or SEQ ID NO:11.

18. The purified polypeptide of claim 17, wherein said functional fragment comprises a fragment that is substantially identical to a polypeptide comprising amino acids 26-34, 51-54, and 91-99 of SEQ ID NO:9 or amino acids 16-22, 40-47, and 86-100 of SEQ ID NO:11.

19. The purified polypeptide of claim 12, wherein said functional fragment comprises a fragment of the sequence of SEQ ID NO:1 or SEQ ID NO:3.

20. The purified polypeptide of claim 12, wherein said functional fragment comprises a fragment of the sequence of SEQ ID NO:5 or SEQ ID NO:7.

21. The purified polypeptide of claim 12, wherein said functional fragment comprises a fragment of the sequence of SEQ ID NO:9 or SEQ ID NO:11.

22. The purified polypeptide of claim 1, 2, 5, 6, 7, or 10, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:1.

23. The purified polypeptide of claim 1, 2, 5, 6, 7, or 10, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:3.

24. The purified polypeptide of claim 1, 3, 5, 6, 8, or 10, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:5.

25. The purified polypeptide of claim 1, 3, 5, 6, 8, or 10, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:7.

26. The purified polypeptide of claim 1, 4, 5, 6, 9, or 10, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:9.

27. The purified polypeptide of claim 1, 4, 5, 6, 9, or 10, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:11.

28. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:1.

29. A purified polypeptide comprising amino acid 26-31, 49-51, and 88-95 of SEQ ID NO:1.

30. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:3.

31. A purified polypeptide comprising amino acids 11-18, 36-43, and 82-90 of SEQ ID NO:3.

32. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:5.

33. A purified polypeptide comprising amino acids 26-34, 52-58, and 97-103 of SEQ ID NO:5.

34. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:7.

35. A purified polypeptide comprising amino acids 11-18, 36-43, and 82-100 of SEQ ID NO:7.

36. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:9.

37. A purified polypeptide comprising amino acids 26-34, 51-54, and 91-99 of SEQ ID NO:9.

38. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:11.

39. A purified polypeptide comprising amino acids 16-22, 40-47, and 86-100 of SEQ ID NO:11.

40. A purified polypeptide comprising the amino acid sequence of SEQ ID NOS:1 and 3.

41. A purified polypeptide comprising amino acid 26-31, 49-51, and 88-95 of SEQ ID NO:1 and amino acids 11-18, 36-43, and 82-90 of SEQ ID NO:3.

42. A purified polypeptide comprising the amino acid sequence of SEQ ID NOS:5 and 7.

43. A purified polypeptide comprising amino acids 26-34, 52-58, and 97-103 of SEQ ID NO:5 and amino acids 11-18, 36-43, and 82-100 of SEQ ID NO:7.

44. A purified polypeptide comprising the amino acid sequence of SEQ ID NOS:9 and 11.

45. A purified polypeptide comprising amino acids 26-34, 51-54, and 91-99 of SEQ ID NO:9 and amino acids 16-22, 40-47, and 86-100 of SEQ ID NO:11.

46. The purified polypeptide of any one of claims 1, 5, 6, 10, or 25-45, wherein said polypeptide is a monoclonal antibody.

47. The purified polypeptide of claim 46, wherein said monoclonal antibody is a human monoclonal antibody.

48. The purified polypeptide of claim 1, 2, 5, 6, 7, or 10, wherein said polypeptide is a polypeptide that is also produced by the PM-1 cell line having DSMZ Accession No. DSM ACC2599.

49. The purified polypeptide of claim 1, 3, 5, 6, 8, or 10, wherein said polypeptide is a polypeptide that is also produced by the PM-2 cell line having DSMZ Accession No. DSM ACC2600.

50. The purified polypeptide of claim 1, 4, 5, 6, 9, or 10, wherein said polypeptide is a polypeptide that is also produced by the CM-2 cell line having DSMZ Accession No. DSM ACC2598.

51. A cell that expresses the polypeptide of claim 1 or 5.

52. A cell that expresses the polypeptide of claim 6 or 10.

53. A cell that expresses a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:1.

54. The cell of claim 53, wherein said polypeptide comprises the sequence of SEQ ID NO:1.

55. A cell that expresses a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:3.

56. The cell of claim 55, wherein said polypeptide comprises the sequence of SEQ ID NO:3.

57. A cell that expresses a polypeptide that comprises the amino acid sequence of SEQ ID NOS:1 and 3.

58. A cell that expresses a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:5.

59. The cell of claim 58, wherein said polypeptide comprises the sequence of SEQ ID NO:5.

60. A cell that expresses a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:7.

61. The cell of claim 60, wherein said polypeptide comprises the sequence of SEQ ID NO:7.

62. A cell that expresses a polypeptide that comprises the amino acid sequence of SEQ ID NOS:5 and 7.

63. A cell that expresses a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:9.

64. The cell of claim 63, wherein said polypeptide comprises the sequence of SEQ ID NO:9.

65. A cell that expresses a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:11.

66. The cell of claim 65, wherein said polypeptide comprises the sequence of SEQ ID NO:11.

67. A cell that expresses a polypeptide that comprises the amino acid sequence of SEQ ID NOS:9 and 11.

68. The cell of any one of claims 51-67, wherein said cell is a hybridoma.

69. A method of generating the cell of claim 51, said method comprising the steps of:

(a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

(b) determining whether said hybridoma produces a polypeptide that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, and

(c) determining whether said hybridoma produces a polypeptide that specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), ASPC-1 (ATCC Accession No. CRL-1682), or BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells.

70. A method of generating the cell of claim 52, said method comprising the steps of:

(a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

(b) determining whether said hybridoma produces a polypeptide that inhibits proliferation in a neoplastic cell to which it binds, but does not inhibit proliferation in a non-neoplastic cell, and

(c) determining whether said hybridoma produces a polypeptide that specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), ASPC-1 (ATCC Accession No. CRL-1682), or BXPC-3 (ATCC Accession No. CRL-1687) cells and not to non-neoplastic cells.

71. Use of the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50 in a method of diagnosing a neoplasm in a mammal, said method comprising the steps of:

(a) contacting a cell or tissue sample of said mammal with the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50 and

(b) detecting whether said purified polypeptide binds to said cell or tissue sample, wherein binding of said purified polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm.

72. The use of claim 71, wherein said mammal is a human.

73. The use of claim 71, wherein said polypeptide is an antibody.

74. The use of claim 71, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

75. The use of claim 71, wherein said polypeptide is conjugated to a protein purification tag.

76. The use of claim 75, wherein said protein purification tag is cleavable.

77. Use of the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell or tissue sample with the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50, wherein binding of said purified polypeptide to said cell or tissue sample results in the induction of apoptosis of said cell or tissue sample.

78. The use of claim 77, wherein said mammal is a human.

79. The use of claim 77, wherein said polypeptide is an antibody.

80. The use of claim 77, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

81. The use of claim 80, wherein said detectable agent is capable of inducing apoptosis of said cell or tissue sample.

82. The use of claim 77, wherein said polypeptide is conjugated to a protein purification tag.

83. The use of claim 82, wherein said protein purification tag is cleavable.

84. Use of the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell or tissue sample with the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50, wherein binding of said purified polypeptide to said cell or tissue sample results in a reduction in proliferation of said cell or of a cell in said tissue sample.

85. The use of claim 84, wherein said mammal is a human.

86. The use of claim 84, wherein said polypeptide is an antibody.

87. The use of claim 84, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

88. The use of claim 87, wherein said detectable agent is capable of inhibiting cell proliferation of said cell or tissue sample.

89. The use of claim 84, wherein said polypeptide is conjugated to a protein purification tag.

90. The use of claim 89, wherein said protein purification tag is cleavable.

91. A medicament comprising the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50 in a pharmaceutically acceptable carrier.

92. A diagnostic agent comprising the purified polypeptide of any one of claims 1, 5, 6, 10, 25-45, 48, 49, or 50.

93. An isolated nucleic acid molecule that is substantially identical to the sequence of SEQ ID NO:2, 4, 6, 8, 10, or 12.

94. An isolated nucleic acid sequence that hybridizes under high stringency conditions to the sequence of SEQ ID NO:2, 4, 6, 8, 10, or 12.

95. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:2, 4, 6, 8, 10, or 12.

96. An isolated nucleic acid molecule, wherein said nucleic acid molecule comprises sequences that are substantially identical to nucleotides 76-93, 145-153, and 262-285 of SEQ ID NO:2.

97. The isolated nucleic acid molecule of claim 96, wherein said nucleic acid molecule comprises nucleotides 76-93, 145-153, and 262-285 of SEQ ID NO:2.

98. An isolated nucleic acid molecule, wherein said nucleic acid molecule comprises sequences that are substantially identical to nucleotides 31-54, 106-129, and 244-270 of SEQ ID NO:4.

99. The isolated nucleic acid molecule of claim 98, wherein said nucleic acid molecule comprises nucleotides 31-54, 106-129, and 244-270 of SEQ ID NO:4

100. An isolated nucleic acid molecule, wherein said nucleic acid molecule comprises sequences that are substantially identical to nucleotides 76-102, 154-174, and 289-309 of SEQ ID NO:6.

101. The isolated nucleic acid molecule of claim 100, wherein said nucleic acid molecule comprises nucleotides 76-102, 154-174, and 289-309 of SEQ ID NO:6.

102. An isolated nucleic acid molecule, wherein said nucleic acid molecule comprises sequences that are substantially identical to nucleotides 31-54, 106-129, and 244-300 of SEQ ID NO:8.

103. The isolated nucleic acid molecule of claim 102, wherein said nucleic acid molecule comprises nucleotides 31-54, 106-129, and 244-300 of SEQ ID NO:8

104. An isolated nucleic acid molecule, wherein said nucleic acid molecule comprises sequences that are substantially identical to nucleotides 76-102, 151-162, and 271-297 of SEQ ID NO:10.

105. The isolated nucleic acid molecule of claim 104, wherein said nucleic acid molecule comprises nucleotides 76-102, 151-162, and 271-297 of SEQ ID NO:10.

106. An isolated nucleic acid molecule, wherein said nucleic acid molecule comprises sequences that are substantially identical to nucleotides 46-66, 118-141, and 256-300 of SEQ ID NO:12.

107. The isolated nucleic acid molecule of claim 106, wherein said nucleic acid molecule comprises nucleotides 46-66, 118-141, and 256-300 of SEQ ID NO:12.

108. A vector comprising the nucleic acid molecule of any one of claims 93-107.

109. A cell comprising the vector of claim 108.

110. A method of preparing the purified polypeptide of claims 1, 5, 6, or 10, said method comprising contacting a cell with the vector of claim 108 and isolating the polypeptide expressed by said cell.